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10/023,427	12/12/2001	Harshal P. Bhagwatwar	U 013528-7	2278

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EXAMINER	
DI NOLA BARON, LILIANA	

ART UNIT	PAPER NUMBER
1615	11

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/023,427	Applicant(s) BHAGWATWAR ET AL.	
	Examiner Liliana Di Nola-Baron	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-68* is/are pending in the application.

4a) Of the above claim(s) *3,9,18-51,53,56-62 and 64-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,10-17,52,54,55 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,9*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claim Rejections - 35 USC § 112

3. Claim 52 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for suppressing serum testosterone (See Example 16), does not reasonably provide enablement for preventing or treating any health disorder, disease or medical condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention is directed to a method of preventing or treating a health disorder, disease or medical condition comprising administering a composition.

(2) The state of the prior art

The state of the art is what prior art knows about the invention. There is no known art, wherein a certain composition is administered to successfully prevent diseases or medical conditions before their occurrence, or to successfully treat any disease.

(3) The relative skill of those in the art

The relative skill of the artisan having a Master degree or Ph.D. in the medical and microbiological arts is high.

(4) The predictability or unpredictability of the art

The unpredictability of diseases is very high. Different diseases may be treated or controlled by administering to the patients affected by said diseases various drug compositions, each effective in treating one particular disease or related diseases. More sensitive patients may be more affected by a disease than others, and may show more symptomatic reactions. There is no known art where a composition comprising a polymer in an organic solvent and an emulsifier in oil is administered to treat any disease or medical condition. Furthermore, there is no known art where a composition is successful in preventing a disease before its occurrence.

(5) The breadth of the claims

The claim is very broad. There is no guidance or disclosure on the disease treated by the composition of the invention. The method reads on a composition (the composition of claim 1), which does not comprise a drug. Thus, the drug is not included in the method of treatment

claimed by Applicant and the disease is not specified. Additionally, no guidance is provided on the dosage of administration.

(6) The amount of direction or guidance presented

The amount of direction and guidance provided by Applicant is limited to a method for suppressing serum testosterone level. There is no evidence in the specification that established correlation between the experiments and the claimed utility of preventing or treating any disease.

(7) The presence or absence of working examples

The working examples present no data on the effect of the compositions of the invention on the prevention of diseases or treatment of medical conditions.

(8) The quantity of experimentation necessary

The effect of the compositions of the invention on the possible prevention and treatment of diseases cannot be predicted a priori but must be determined from the case to case by painstaking experimental study in vivo. When the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine a possible preventive and therapeutic effect of the method claimed in the instant application.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Regarding claim 7, the phrase "genetic material" renders the claim indefinite, because it is not clear how said material differ from the DNA fragments and nucleic acids recited in the claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 2, 5-8, 11-17, 52, 54, 55 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawhney (U.S. Patent 6,632,457).

Sawhney discloses hydrogel microspheres formed from polymerizable macromers or monomers by dispersion of a polymerizable phase in a second phase (See col. 7, lines 13-20).

With respect to claim 1 of the instant application, Sawhney discloses injectable compositions in the form of microspheres or microdroplets dispersed in a hydrogel matrix and formed in situ, and comprising compounds in solution in another phase, which is immiscible with the hydrogel

phase (See col. 8, lines 1-49 and col. 12, lines 5-35). The microdlopets disclosed by the prior art are a microcarrier delivery system, as claimed by Applicant. With regard to the droplet-in-oil dispersion claimed by Applicant, Sawhney teaches oil droplet reservoirs in the hydrogel matrix comprising a dispersion of a water-soluble drug in the form of microspheres, wherein the oil phase includes a release rate modifying agent (See col. 128, lines 46-55). Sawhney contemplates biodegradable polymers to form the hydrogel compositions of the invention (See col. 2, lines 50-60), as well as solvents to form microspheres (See col. 13, lines 51-60). Additionally, Sawhney teaches the presence of release rate modifying agents, and specifically sorbitan monostearate, in the oil phase (See col. 14, lines 10-19 and col. 16, lines 59-60). Sawhney is deficient in the sense, that it does not specifically teach that the controlled release microcarrier is formed when the dispersion comes into contact with an aqueous fluid, however, the reference teaches that the microdroplets may be formed in situ (See col. 7, lines 11-12). One of ordinary skill in the art would interpret the phrase "in situ" as "the site of application in the body", and thus in the presence of biological fluid.

With regard to claim 2, Sawhney includes polylactic acid and copolymers of lactic and glycolic acid (PLGA) among the polymers used to form biodegradable microspheres (See col. 2, lines 50-61).

Regarding claims 5, 54 and 55, Sawhney teaches that any pharmaceutically acceptable oil may be used, including peanut, castor, coconut and corn oil (See col. 13, lines 37-39).

Regarding claim 6, Sawhney teaches the presence of sorbitan monostearate in the compositions of the invention as capable to form a stable dispersed phase within the hydrogel matrix (See col. 14, lines 10-19 and col. 16, lines 59-60) . The burden is shifted on Applicant to show that the sorbitan monostearate disclosed by the prior art would not be capable of gelling the solvent and the oil, as claimed by Applicant.

With respect to claims 7, 8 and 63, Sawhney includes anesthetics, such as lidocaine, peptides, analgesics, antibiotics and antitumor agents among the drugs delivered by the carrier of the invention (See col. 10, line 49 to col.11, line 54).

With regard to claim 11, the reference teaches that the microdroplets may be formed in situ (See col. 7, lines 11-12). One of ordinary skill in the art would interpret the phrase "in situ" as "the site of application in the body", and thus in the presence of biological fluid. In fact, Sawhney teaches that the particles accumulate in the lungs, liver and spleen (See col. 18, line 60 to col. 19, line 2).

With regard to claims 12 and 13, Sawhney does not specifically teach the concentration of the polymer and emulsifier in the compositions of the invention, however, one of ordinary skill in the art would have been capable of determining the optimal concentration by routine experimentation.

Regarding claim 14, Sawhney teaches that the microspheres (i.e. the microcarriers) of the invention may be in the form of sphere, droplet or other particle irregular shape (See col. 12, lines 18-22).

With respect to claims 15-17, Sawhney discloses particles ranging in size between 1 and 10 microns (See col. 12, lines 64-65).

With regard to claim 52, Sawhney teaches administering the delivery systems of the invention (See col. 8, lines 30-49) and provides methods to enhance the targetability of microencapsulated drug and carriers, so that they act as therapeutic entities (See col. 6, lines 56-59 and col. 18, line 60 to col. 19, line 31).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Sawhney to device compositions for forming microcarriers and methods of treatment comprising administering said compositions. Because of the teachings of Sawhney, that the microspheres of the invention may be formed in situ from phase dispersions, one of ordinary skill in the art would have a reasonable expectation that the compositions and method claimed in the instant application would be successful in providing a microcarrier controlled delivery system for drugs and therapeutic methods. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

9. Claims 4 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawhney as applied to claims 1, 2, 5-8, 11-17, 52, 54, 55 and 63 above, and further in view of Borisy et al. (U.S. Patent 6,569,853).

The teachings of Sawhney have been summarized above. With respect to claim 4, while Sawhney discloses organic solvents, such as DMSO, in the compositions of the invention (See col. 13, lines 5060), the reference fails to specifically include NN' dimethylacetamide, as claimed by Applicant. With regard to claim 10, Sawhney teaches antitumor agents (See col. 11, lines 45-54), however, the reference fails to specifically mention paclitaxel.

With respect to claim 4, Borisy et al. discloses DMSO and NN' dimethylacetamide as equivalent in the art (See col. 18, lines 34-38).

With regard to claim 10, Borisy et al. teaches that the most commonly used anticancer agent is paclitaxel, which is used alone or in combination with other antitumor agents (See col. 1, lines 38-46). The antitumor agents disclosed by Borisy et al. are also disclosed by Sawhney (See col. 11, lines 46-54).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the compositions disclosed by Sawhney, by including paclitaxel among the antitumor agents delivered by the microcarrier of the invention, and NN' dimethylacetamide among the organic solvents. Because of the teachings of Sawhney, that the

microcarriers of the invention can be used for controlled delivery of antitumor agents, and the teachings of Borisy et al., that paclitaxel is the most common anticancer drug, one of ordinary skill in the art would have a reasonable expectation that the compositions claimed in the instant application would be successful in providing a microcarrier controlled delivery system for anticancer drugs, such as paclitaxel. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

November 20, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600